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Association of CUN-BAE, BRI and Hypertension among Adolescents Aged 12-18 Years in US, NHANES, 1999-2018

Abstract

Background: CUN-BAE (The Clínica Universidad de Navarra-Body Adiposity Estimator index) and BRI (Body Rounds Index) are associated with adult's hypertension. We aimed to assess whether CUN-BAE, BRI is associated with the prevalence of hypertension in adolescents and whether it is superior to Body Mass Index (BMI).

Methods: 12,605 adolescents aged 12-18 years were enrolled from the National Health and Nutrition Examination Survey (NHANES). Correlations between CUN-BAE, BRI and the prevalence of hypertension in adolescents were analysed using logistic regression. Receiver Operating Characteristic curve (ROC curve) was used to predictive value for the prevalence of hypertension in adolescents.

Results: CUN-BAE, BRI, BMI were positively associated with the prevalence of hypertension in adolescents (The multivariable OR (95%CI): 4.47 (3.44-5.82), for CUN-BAE, 2.95 (2.38-3.66) for BRI and 3.97 (3.11-5.07) for BMI, for quartiles 4 *versus* quartile 1, respectively) and the relationship was monotonically increasing ($p<0.001$ for all trends). The effects of CUN-BAE, BRI and BMI on hypertension were more pronounced in participants aged 15-18 years. Significant association between CUN-BAE and prevalence of hypertension in adolescents observed only in male. BRI had more significant effects on hypertension in female. CUN-BAE and BRI did not show significant superiority over BMI in predicting the prevalence of hypertension in adolescents.

Conclusions: CUN-BAE and BRI were significantly and positively associated with the prevalence of hypertension in adolescents, especially among participants aged 15 years and older. But they were not a substitute for BMI. CUN-BAE and BRI were unique in the risk of hypertension in adolescents.

Keywords: CUN-BAE; Body rounds index; BMI; Hypertension; NHANES

Abbreviations: CUN-BAE: Clínica University of Navarra -Body Fat Estimator; BRI: Body Rounds Index; BMI: Body Mass Index; NHANES: National Health and Nutrition Examination Survey; ROC: Receiver Operating Characteristic; ORs: Odds Ratios; CIs: Confidence Intervals; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BP: Blood Pressure; WC : Waist Circumference; HDL: High Density Lipoprotein; HTN: Hypertension; HbA1c: Hemoglobin A1C; CDC: Centers for Disease Control and Prevention; SE: Standard Errors; RCS: Restricted Cubic Spline

Introduction

Elevated blood pressure and hypertension commonly occur in children and adolescents and increase the risk of cardiovascular disease in adulthood [1]. A systematic review and meta-analysis reported that the global prevalence of prehypertension and hypertension were clearly increasing from 1994 to 2018 among those ≤ 19 years of age [2]. A national survey in the United States showed that an estimated 7.1% of children and adolescents aged 8-17 years had elevated blood pressure and 3.5% had hypertension between 2013 and 2016 [3]. Identifying hypertension earlier in life can have significant benefits across an individual's lifespan [4]. Therefore, it was a great public health significance that conduct research on hypertension in children and adolescents.

Hypertension is more common in adolescents undergoing puberty and children who were overweight or obese [2]. In obese children, the prevalence of arterial hypertension is much higher than in normal-weight children and weight gain accounts for 75 per cent of the risk of primary hypertension [5]. In epidemiological studies, it has been observed that BMI and other markers of fatness can help to identify children with elevated blood pressure [6]. To date, BMI is the most widely used parameter to assess overweight and obesity. However, some studies suggested that BMI is not effective in assessing body fat or obesity, as it does not provide information on the distribution of body fat and does not take into account lean body mass and

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important factors associated with obesity, especially age, gender or race [7,8]. In other words, even patients with a normal BMI but low lean body mass and a relatively high distribution of visceral fat may have elevated blood pressure with typical metabolic abnormalities [6].

Therefore, new practical adiposity indexes have been proposed. The CEU-BAE was proposed for estimating body fat percentage, taking into account BMI, sex and age [8]. The CUN-BAE index may help detect individuals who are of normal weight according to BMI, but are metabolically unhealthy [9,10]. The BRI is a tool that measures body fat and visceral fat and was first introduced in 2013 [11]. The BRI may be more useful than other anthropometric indices because of its ability to reflect height-related body roundness (abdominal obesity) and to more accurately estimate body fat percentage and visceral fat percentage [11]. In addition, several observational studies have demonstrated an association between BRI and hypertension or elevated blood pressure in adult [12,13]. Height, waist circumference and adipose tissue distribution characteristics of adolescents are influenced by age and sex. To the best of our knowledge, no studies has explored whether CUN-BAE or BRI are better predictor of hypertension in adolescents than BMI.

The aim of this study was to investigate the association between CUN-BAE, BRI and the prevalence of hypertension in adolescents and whether CUN-BAE and BRI are better than BMI in predicting the prevalence of hypertension in adolescents.

Materials and Methods

Study population

All the databases could be obtained from the NHANES website, which was a nationally representative survey of nutrition and health condition in the United States. We analysed the data from 10 cycles (1999-2018). A total of 101,316 subjects were enrolled at first, after excluding those younger than 12 and older than 18 years (86,059), those with missing physical measures (961), those with missing information on blood pressure measurements (1,303) and those with missing dietary sodium intake (388). We finally included 12,605 participants in this study.

Definition of variables

Hypertension: We defined hypertension according to the 2017 American Academy of Pediatrics clinical practice guidelines [14]. We used Systolic/Diastolic Blood Pressure (SBP/DBP) percentile tables to define hypertension based on sex, height and age, for children aged 1-12 years: (1) "Normal BP" was defined as SBP and DBP values<90th percentile. (2) "Elevated BP" was defined as SBP and/or DBP ≥ 90th percentile to <95th percentile or 120/80 mm Hg to<95th percentile. (3) "Stage 1 HTN": ≥ 95th percentile to<95th percentile+12 mm Hg or 130/80 to 139/89 mm Hg. (4) "Stage 2 HTN": ≥ 95th percentile+12 mm Hg or ≥ 140/90 mm Hg. For children aged more than 13 years:(1) "Normal BP" was defined as SBP and DBP values<120/<80 mm Hg. (2) Elevated BP: 120/<80 to 129/<80 mm Hg. (3) Stage 1 HTN: 130/80 mm H g to 139/89 mm Hg. (4) Stage 2 HTN: ≥ 140/90 mm Hg.

Clinica universidad de navarra-body adiposity estimator index

We calculated the CUN-BAE index with the equation proposed by Gomez-Ambrosi et al., [8]. CUN-BAE: $-44.988+(0.503 \times \text{age})+(10.689 \times \text{sex})+(3.172 \times \text{BMI})-(0.026 \times \text{BMI}^2)+(0.181 \times \text{BMI} \times \text{sex})-(0.02 \times \text{BMI} \times \text{age})-(0.005 \times \text{BMI}^2 \times \text{sex})+(0.00021 \times \text{BMI}^2 \times \text{age})$, where age was measured in years and sex was codified as men =0 and women=1.

Body roundness index: BRI was computed by $364.2-365.5^{*}(1-(\text{WC(m)}/2\pi)^2/(0.5^{*}\text{height(m)})^2)^{½}$ [11].

Body mass index: BMI was calculated as measured weight (kg) divided by the square of height (m^2) and then converted to sex- and age-specific BMI percentile values using a computerized formula derived from the 2,000 centers for disease control growth charts [15]. Participants were allocated to one of three BMI categories: Obesity (≥ 95th percentile), overweight (85th to 94th percentile) or normal or below (<85th percentile).

Covariates: Potential confounding factors for adjustment were age (12~14, 15~18) [16], sex (male, female), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black and other race-including multi-racial), secondhand smoke (<0.03, 0.03~3, >3), poverty level (<1.3, ≥ 1.3), total cholesterol (<200, 200~400, ≥ 240) and triglyceride (<150, ≥ 150), HDL (<40, 40~60, ≥ 60), HbA1c (≤ 6.5, >6.5), sodium (continuous), total fat (continuous), calcium (continuous), magnesium (continuous), potassium (continuous).

Statistical analyses

All statistical analyses were conducted according to Centers for Disease Control and Prevention (CDC) guidelines and an appropriate NHANES sampling weight was applied and accounted for complex multistage cluster survey design in the analysis [17]. Means and Standard Errors (SE) were used for quantitative variables (sodium, *etc.*). Categorical variables were presented as number (N) and percentage (%). T-tests and Chi-square (χ^2) test were used for comparisons between groups. The Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of prevalent hypertension were calculated using the logistic regression analysis according to CUN-BAE/BRI/BMI. Missing values for these covariates were treated as additional missing categories and their indicators dummy variables were included into the model. Stratified analyses by age (12 to 14, 15 to 18) and sex (male, female) were presented with a fully adjusted Model 3. The non-linear relationships between CUN-BAE, BRI, BMI levels and hypertension were assessed using Restricted Cubic Spline curve (RCS curve). Predictive value of CUN-BAE, BRI and BMI for prevalence of hypertension in adolescents assessed using ROC curve. We used SAS version 9.4 software (SAS Institute Inc, Cary, NC, USA) in all statistical analyses. Figures 1 and 2 were drawn by R version 4.4.2 software. Two-tailed p-values of <0.05 were considered statistically significant.

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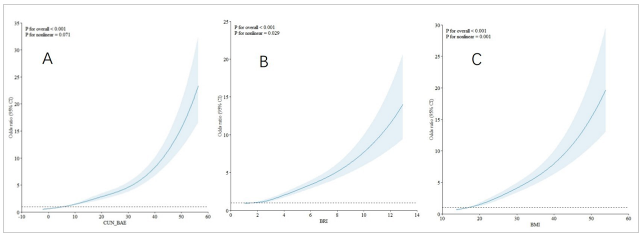

Figure 1: Restricted cubic spline fitting for the association between adjusted for age, sex, race, secondhand smoke, sodium, magnesium, cholesterol-total, triglyceride, HDL. **Note:** A) CUN-BAE *vs*. odds ratio; B) BRI *vs*. odds ratio; C) BMI *vs*. odds ratio levels with hypertension.

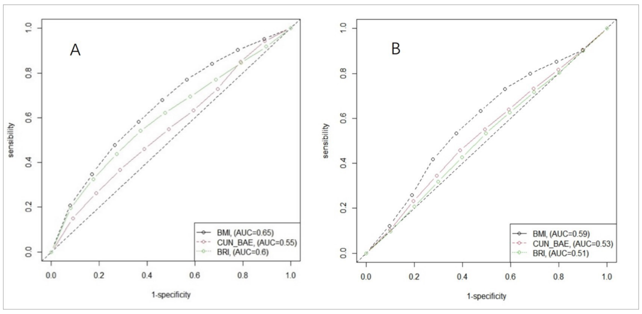

Figure 2: ROC curves for CUN-BAE, BRI and BMI to predict the prevalence of hypertension in adolescents. **Note:** A) Unadjusted; B) Adjusted.

Result

Supplementary Tables 1-3 shows weighted baseline characteristics of study participants according to hypertension status. Among 12,605 participants (6,405 males and 6,200 females) aged 12-18 years, the respective proportions of hypertension and non-hypertension were 15.49% and 84.51%. Compared with adolescents with non-hypertension, those in the hypertensive group were older, had higher proportions of males, Mexican Americans/non-Hispanic blacks, overweight/obesity, intermediate/heavy exposure to secondhand smoke >0.03 ng/ml, total-cholesterol >200 mg/dL, triglycerides >150 mg/dL and HDL<40 mg/dL and had higher levels of magnesium, BRI and CUN-BAE.

Supplementary Table 4 shows the association between CUN-BAE, BRI, BMI and hypertension in adolescents. After adjusting for confounding factors, CUN-BAE, BRI and BMI were positively associated with the prevalence of hypertension in adolescents. In addition, to ensure the stability of the results, a trend test was carried out in this study. CUN-BAE, BRI and BMI were converted from continuous variables to categorical variables and divided according to quartiles of CUN-BAE, BRI and BMI. The risk showed a dose-response pattern in CUN-BAE, BRI, BMI groups (The multivariable OR (95%CI): 4.47 (3.44-5.82) for CUN-BAE, 2.95 (2.38-3.66) for BRI and 3.97 (3.11-5.07) for BMI, for quartiles 4 *versus* quartile 1, respectively, p<0.001 for all trends).

The results of the subgroup analysis by age and sex are shown in Figure 3 the p-values for interactions between CUN-BAE, BRI, BMI and age were <0.001 for hypertension. CUN-BAE, BRI and BMI had a more signi icant effect on hypertension in participants aged 15-18 years than in those aged 12-14 years. The p-values for interactions between CUN-BAE, BRI and sex were <0.05 for hypertension. CUN-BAE had more signi icant effects on hypertension in male. BRI had more signi icant effects on hypertension in female. We found a "J" shape relationship between CUN-BAE, BRI, BMI and hypertension in adolescents, as shown in Figure 1. The RCS curve show that the prevalence of hypertension in adolescents increases with increasing levels of CUN-BAE, BRI and BMI. **Figure 3** show the effectiveness of CUN-BAE, BRI and BMI in predicting the prevalence of hypertension in adolescents. BMI (AUC:0.59) was signi icantly better than CUN-BAE and BRI in predicting the prevalence of hypertension in adolescents.

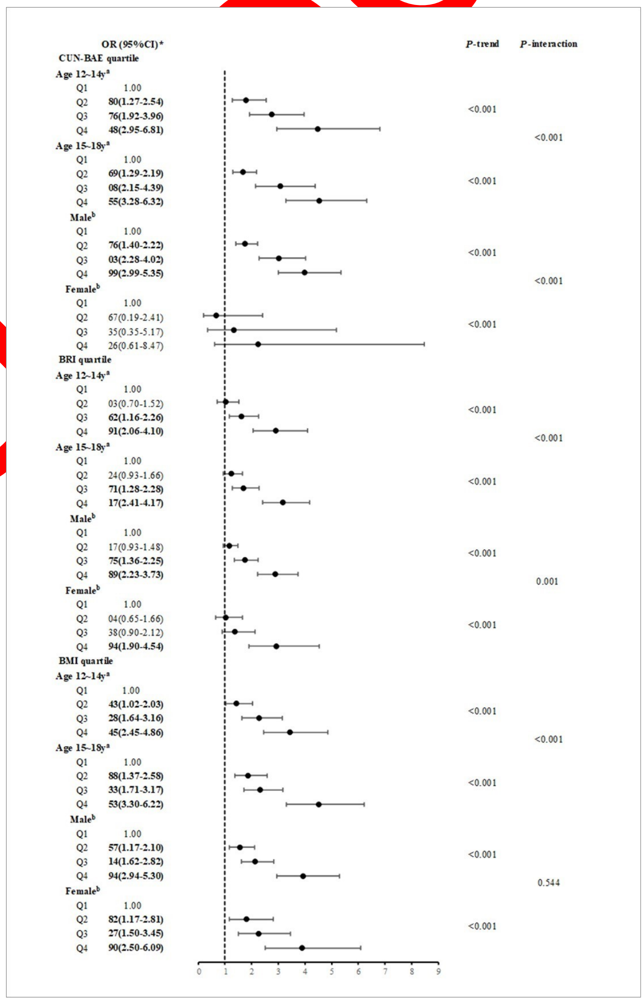

Figure 3: Association between CUN-BAE, BRI, BMI and hypertension in adolescents strati ied by age and sex.

Discussion

In this study of NHANES data from a nationally representative sample of U.S. adolescents aged 12 to 18 years, we found that CUN-BAE and BRI were positively associated with hypertension in adolescents and the prevalence of hypertension was higher in adolescents older than 15 years of age. The positive association between CUN-BAE and prevalence of hypertension was evident for males. However, the positive association between BRI and prevalence of hypertension was more pronounced for females. We also found BMI was significantly better than CUN-BAE and BRI in predicting the prevalence of hypertension in adolescents. To our knowledge, this was the first study of its kind in American children and adolescent.

Our result was similar with the previous studies based on adult. A prospective cohort study of adults with a follow-up time of 12.3 years found a strong direct association between progressively higher baseline CUN-BAE and the prevalence of hypertension during the follow-up period in both men and women, even after further adjustment for BMI ≥ 30 kg/m^2 [18]. Another cross-sectional study representing a Spanish adult population found that CUN-BAE was positively associated with the risk of hypertension in adults and that the OR of CUN-BAE was significantly higher than BMI or waist circumference in both sexes [19]. Our findings also showed that BMI was significantly better than CUN- BAE in predicting the prevalence of hypertension in adolescents. However, a cross-sectional study of adults aged >8 years old found that the CUN-BAE showed a better gradient of association with hypertension and diabetes than BMI. The population attributable fraction for arterial hypertension was double when assessed with CUN-BAE as compared to BMI, while for DM it was more than 50% higher [20]. That result was different from our finding may be due to differences in the study population (adults *vs*. adolescents). The CUN-BAE indicator is a formula calculated on the basis of data for adults however, it is not specifically adjusted and calculated for the adolescent population. Therefore, more studies are needed to further validate the prediction of CUN-BAE on the incidence of hypertension in adolescents.

In addition, it has been reported that for a given BMI, men have more lean mass and women have higher adiposity [21]. Body proportions and fat distribution change during the pubertal years. For example, girls reach peak calcium accretion around 12.5 years of age, whereas boys reach this stage at about 14 years. Boys gain greater amounts of fat free mass and skeletal mass during puberty, whereas girls acquire significantly more fat mass [22]. However, women have more subcutaneous adipose tissue, while men have fat, predominantly distributed to the visceral adipose tissue around the abdominal organs [23]. Girls tend to accumulate more total body fat and subcutaneous adipose tissue during and after puberty, depositing fat preferentially in the gynoid and extremity regions, while pubertal and post pubertal boys tend to deposit more fat in the abdominal region, particularly in the visceral adipose tissue depot [24]. An investigation of changes in the amount of visceral adipose tissue carried out by Fox et al., among the same children aged 11 and 13 years showed that for boys there was a mean percentage increase in waist scan area of 8%. This was accompanied by an increase of 69% in intra-abdominal fat area but only 19% increase in subcutaneous fat area [25]. Inflammatory changes within the visceral adipose tissue with leukocyte accumulation and activation have been strongly associated with metabolic disease [26]. The subcutaneous adipose tissue is associated with very little inflammation during obesity and is more avid in absorption of circulating free fatty acids and triglycerides and can actually provide a protective effect against obesity-related diseases [27]. In addition, according to the report, with the increase in adipose tissue mass and the altered distribution pattern caused by age change, women had a lower risk of hypertension than men at young age, but the opposite was the case at postmenopausal age [28]. The CUN-BAE, which additionally takes into account the risk of hypertension in menopausal women, may introduce uncertainty in assessing the risk of hypertension in children and adolescents. This could explain our findings that the association between CUN-BAE and hypertension was significant in male adolescents not in female.

A retrospective analysis in Japan showed that BRI were significantly associated with the prevalence of hypertension in both men and women across all age categories from 30s to 60s [29]. Similarly, the increased BRI was also observed to be associated with an increased risk of hypertension in Chinese individuals, according to a cohort study from China Health and Nutrition Survey (CHNS) [30]. Our results were consistent with the previous findings. In addition, previous studies showed that BRI was very good predictor of hypertension. A cross-sectional study in the United States reported that BRI demonstrated significant discriminatory abilities for hypertension in adult [31]. However, the results of present study showed that BRI was not as good as BMI in predicting the prevalence of hypertension in adolescents. This may be related to the BRI's inability to accurately describe visceral adipose tissue in children and adolescents. The BRI was designed to determine both the amount of visceral adipose tissue and body fat using WC in relation to height, which allows estimation of the shape of the human body figure as an oval or ellipse [11,32]. Because the accumulation of visceral adipose tissue in children is influenced by genetic factors, ethnicity, growth, puberty and maturation [33]. In children and adolescents, total body fat, visceral adipose tissue and subcutaneous adipose tissue typically increase as a child ages, though different trends emerge [24].

Therefore, the BRI, may not accurately descript condition of adiposity dynamics in children and adolescents, has predictive value for hypertension in adolescents, but may not be superior to traditional indicators.

A rural Chinese cohort study showed that the people who was metabolically healthy while abdominal obesity was associated with increased risk of hypertension [34]. Although the mechanisms of the association between abdominal obesity and hypertension were not clear, presently. A study suggest that excess visceral fat is causally related to metabolic abnormalities resulting in increased insulin resistance, that could result in a decreased ability of insulin to mediate vasodilatation in vascular tissue resulting in increased blood pressure [35]. On the other hand, the mechanisms by which obesity leads to hypertension is thought to be related to inflammation caused by excessive adiposity accumulation, especially visceral fat deposition [36]. Visceral fat is an important site for IL-6 secretion and visceral fat adipokine secretion is associated with systemic inflammation in obese humans [37]. Several studies suggest that low-grade inflammation plays a key role in triggering and maintaining high blood pressure [38,39]. In addition, abdominal adiposity was positively associated with arterial stiffness, which further lead to hypertension [40].

The strengths of our study are several. First, we used high-quality, representative data on U.S. adolescents from the NHANES, which is large and multistage. Second, as far as we know, we are the first to examine the association between CUN-BAE, BRI and the prevalence of hypertension in adolescents and the large sample size is another advantage of this study.

We declare several potential limitations in our study. First, an inherent limitation of the CUN-BAE calculation is that the formula was established on samples taken from the adult population and thus a great deal of research is needed to conduct to explore a correction formula appropriate for adolescents. Second, although we adjusted for multiple covariates, we were unable to completely rule out the effects of other confounding factors on the results. Finally, determining a causal relationship between CUN-BAE, BRI and hypertension in adolescents is challenging due to the inherent nature of cross-sectional studies. Further prospective studies are needed to determine the exact relationship between different forms of obesity assessment indicators and hypertension in adolescents.

Conclusion

CUN-BAE and BRI were significantly and positively associated with the prevalence of hypertension in adolescents, especially among participants aged 15 years and older. CUN-BAE and BRI did not show significant superiority over BMI in predicting the prevalence of hypertension in adolescents. However, when compared to BMI (Body Mass Index), neither CUN-BAE nor BRI showed a significant advantage in predicting hypertension risk. This suggests that while alternative measures like CUN-BAE and BRI may provide additional insights into hypertension risk, BMI remains a reliable and comparable tool for identifying adolescents at higher risk for hypertension.

Declarations

Ethics approval and consent to participate

Data collection for the NHANES was approved by the NCHS Research Ethics Review Board (ERB). An individual investigator utilizing the publicly available NHANES data do not need to file the institution Internal Review Board (IRB).

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